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Retinal and choroidal vascular changes in coronary heart disease: an optical coherence tomography angiography study

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Abstract: To reveal the association between retinal microvasculature changes and coronary heart disease (CHD), we assessed the full retinal thicknesses of eight areas, the vessel density of four layers (consisting of nine areas) and the flow area in two layers with optical coherence tomography angiography (OCTA) in CHD patients and healthy controls. The mean vessel density of several layers was significantly lower in patients. The difference in choroid capillary flow (negative correlation) between the two groups was significant. Decreased vessel density and blood flow were associated with coronary artery and branch stenosis. The decreases in retinal vessel density, choroidal vessel density, and blood flow area are closely related to coronary artery and branch stenosis.

1. Introduction

Coronary heart disease (CHD) is the leading cause of morbidity and mortality globally [1,2]. Precipitating factors of CHD include atherosclerosis (most common), vasospasm, and a progressive chronic inflammatory process of arterial wall thickening or stenosis [3]. Several studies have shown a potential correlation between the coronary artery and many peripheral vessels in the human body, such as the cerebral, renal, and ocular vasculature [4–6].

The human retina (ten layers) is supplied by two vascular beds (retinal vessels and choriocapillaris). Retinal vessels supply the inner five layers and accommodate visual function. The outer five layers of the retina are almost avascular, receiving oxygen and nutrients from the choroidal circulation. Thereinto, a large capillary network beneath the retina, referred to as choriocapillaris, enhances the transport. Because fundus vessels are approximately the same magnitude as the coronary microvasculature, they can serve as a representative of processes occurring in subclinical coronary stenosis [7]. Both retinal and choroidal vessels are supplied by the ophthalmic artery (OA), one of the terminal branches of the coronary artery. In other words, the retina and choroid may be affected by coronary artery stenosis. The retinal microvasculature has been proposed as an easily measured surrogate for the coronary circulation in several pieces of literature even though there is still conflicting evidence as to the strength of evidence [7].

Fortunately, due to the unique structure of the eyeball, fundus vasculopathy can be detected accurately by particular examination methods. Traditional techniques for evaluating vasculopathy in a clinical setting include ophthalmoscopy, funduscopy, fundus photography, and fundus fluorescein angiography (FFA). Despite the increasing inconvenience of the procedure (intravenous injection) and the side effects of fluorescein, FFA has been regarded as the "gold standard" in the analysis of vascular and capillary beds for more than five decades [8]. In recent years, optical coherence tomography angiography (OCTA), a new-style noninvasive imaging technology, has been used in clinical practice. This novel diagnosis tool

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can directly evaluate and quantify vascular density or blood flow at different fundus anatomical layers [9,10]. It has been used as an accessible early diagnostic tool for multiple ocular angiopathies, such as age-related macular degeneration (AMD) [11–13], diabetic retinopathy (DR) [8,14] and hypertensive retinopathy [5,15].

Previous studies have provided limited data supporting the association between retinal microvasculature changes and coronary artery disease (CAD) or CHD. Tabatabaee et al. found retinal arterial atherosclerosis was strongly correlated with the extent and severity of CAD by using fundus photography [5]. Wong TY et al. found the correlation between retinal arteriolar narrowing and the incident/development of CHD by measuring the diameters of individual arterioles and venules on retinal photographs [16]. However, to the best of our knowledge, no study has revealed the association between CHD and retinal/choroidal vascular changes by using OCTA. In this study, patients were all diagnosed with CHD by coronary angiography (CAG). Therefore, the aim of our study focused on the retinal and choroidal vascular changes in CHD participants.

The purpose of this study was to investigate the vessel density and blood flow on the retina and choroid by OCTA in patients with CHD, as well as to answer the two questions: First, whether the fundus (retina and choroid) vessel structure and microcirculation changes can implicate early lesion of the coronary artery, and second, whether OCTA can reveal ophthalmic risk factors in CHD patients.

2. Methods

This prospective, cross-sectional observational research was performed at the Department of Cardiology, Ninth People's Hospital, Shanghai Jiaotong University, School of Medicine and Department of Ophthalmology, Huashan Hospital, Fudan University, from January 1, 2017, to December 31, 2017. Written informed consent was obtained before screening for all participants.

2.1 Subjects

A total of 158 patients with CHD (group A, study group) and the same number (158) of healthy subjects (group B, control group) were recruited. All participants underwent a comprehensive ophthalmologic examination consisting of visual acuity (best corrected visual acuity (BCVA), intraocular pressure (IOP), and slit-lamp biomicroscopy combined with retinoscope. Average blood pressure and blood glucose levels were also obtained if participants had a history of hypertension or diabetes. Evaluation criteria included Keith-Wagener-Barker classification (hypertensive retinopathy) and Early Treatment Diabetic Retinopathy Study level 10 (diabetic retinopathy).

Inclusion criteria for group A included (1) definite diagnosis of CHD; (2) normal blood pressure or glucose (hypertension and diabetic participants with successful medical control was also involved) with no hypertensive or diabetic retinopathy on the basis of clinical examination by slit-lamp biomicroscopy and indirect ophthalmoscopy, normal IOP (10-21 mmHg) and BCVA (>6/7.5); (3) no history of major retinal surgery or treatment, such as panretinal photocoagulation (PRP) or pars plana vitrectomy; (4) no severe cataract and no macular pathology, such as epiretinal membrane, vitreomacular traction, and age-related macular degeneration; (5) refractive error less than ± 3.0 D. For group B, the inclusion criteria were the same, except that the subjects had no history of any systemic diseases that may affect fundus vessels. CHD patients with moderate and high myopia/hyperopia (≥ ± 3 diopters or axial length ≥ 26 mm), any kind of glaucoma, dioptric media opacity that may affect OCTA imaging and a history of any intraocular surgery or other fundus diseases were excluded. Patients with firm evidence of macular edema were also excluded. The control subjects in group B had a BCVA of 16/20 or better and underwent an ophthalmic examination to exclude glaucoma, cataract and fundus diseases, or other systemic diseases.

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2.2 Coronary artery angiography (CAG) and Gensini score

All participants underwent coronary artery angiography (CAG) examination during the study period by the same blinded, experienced cardiologist using Philips Allura Xper FD20 biplane fluoroscopy system (Koninklijke Philips Healthcare, Cambridge, Massachusetts, USA). Stenosis of each coronary artery branch was recorded, and the Gensini score was calculated according to this record.

Gensini score has been widely used in routine screening for the severity of coronary artery disease [17,18]. According to Gensini score, 1% to 25%, 26% to 50%, 51% to 75%, 76% to 90%, 91% to 99% and 100% (totally occluded) of stenosis in the lumen of coronary arteries represent the stenosis degree scores of 1, 2, 4, 8, 16 and 32, respectively. This score is then multiplied by the segment location multiplying factor based on the location of the lesion along the coronary artery. The score of 5 is assigned for the left main coronary artery (LMCA), whereas 2.5 is assigned for the proximal left anterior descending (LAD) and left circumflex (LCX). The scores of 1.5 and 1.0 were given to the mid-LAD and the middle/distal segments of LCX, respectively. The lesions involving the obtuse marginal (OM), right coronary artery (RCA) and posterior descending arteries (PDA) are generally multiplied by the score of 1.0. Method of calculating the Gensini was according to the guideline of Gensini G. G in 1983 [17].

2.3 Optical coherence tomography angiography Imaging

The retinal and choroidal images were captured by an AngioVue OCT instrument (wavelength: 840 nm; Optovue, Fremont, CA, USA) and Avanti System (version 2016.1.0). Optovue AngioVue software (version 2016.1.0, Optovue, Fremont, CA, USA) was used to perform measurements.

Retinal thickness was defined as the height from the internal limiting membrane (ILM) to retinal pigment epithelium (RPE). The parafoveal region was the circle with fovea center and 1 mm diameter except for the fovea. Another annulus surrounding the fovea (with an internal and external diameter of 1 and 3 mm, respectively) was further divided into quadrants with two diagonal lines (superior, inferior, nasal, and temporal). We also brought the superior and inferior-hemi value into the study. Finally, a total of nine areas of density (whole image, fovea, parafovea, superior-hemi, inferior-hemi, superior, inferior, nasal and temporal) were available for analysis. These zones were partitioned automatically by using the AngioVue OCT software (version 2016.1.0, Optovue, Fremont, CA, USA), then artificially adjusted according to the actual situation of the picture by the same examiner. A schematic of the examined zones is presented in Fig. 1.

The retinal thickness was measured along 24 horizontal and 24 vertical lines. The number of frames used was reported in the averaging for each line, each of which was 3 mm long and centered at the fovea. Forty-eight frames were averaged together with the aid of eye tracking, and images with a signal strength index (SSI)>39 were selected. The lines crossing the foveal region were automatically calculated and converted to foveal thickness by using AngioVue OCT software (version 2016.1.0, Optovue Inc, USA). For the remaining areas, the average retinal thickness was calculated as the weighted average of all thickness measurements in the region. Vessel density and flow area were measured in four layers (superficial, deep, outer, choroid capillary) and two layers (outer, choroid capillary), respectively. Each scan region was further divided into sectors, the same as retinal thickness described above (the circle area of flow was 3.142 mm^2). The superficial setting (for the superficial plexus) was defined as approximately 3 μm below the ILM to 15 μm below the inner plexiform layer (IPL). The deep setting (for the deep plexus) was defined as 15 to 70 μm below the IPL with an approximate thickness of 55 μm. The outer retina setting was defined as 70 μm below the IPL and 30 μm below the RPE reference line (RPE ref). The choroid capillary setting (for the choroid capillaries) was defined as 30 μm below the RPE ref to 60 μm below the RPE ref with an approximate thickness of 30 μm (Fig. 1). The software automatically fitted the

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designated margins and measured the vessel density. Two blinded, independent examiners then reassessed data. A third blinded investigator made the final decision if disagreements and discrepancies in the assessments arose.

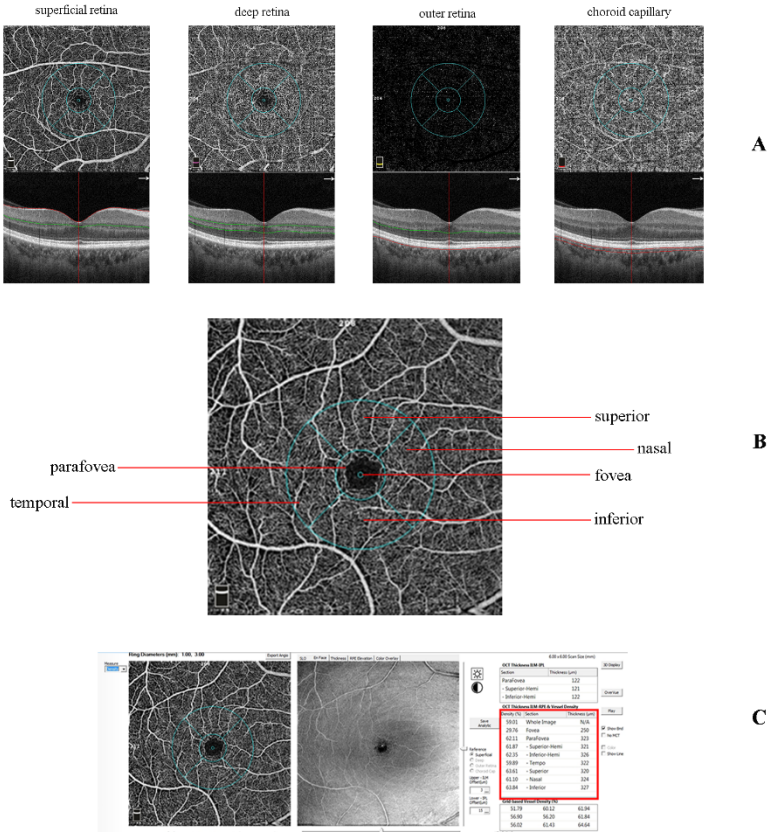

Fig. 1. Different layers on the retina examined by OCTA and corresponding parts in the thickness map, including the superficial, deep, outer retina and choroid capillary (A). Areas on the right eye examined by OCTA included the fovea, parafoveal circle, and superior, inferior, temporal, and nasal areas (B). Retinal thickness and vessel density chart, in which averages of retinal thickness (except in the whole image) and vessel density measurements of nine areas are calculated and automatically displayed (red frame) (C).

2.4 Statistical analysis

Statistics were calculated using SPSS software (IBM SPSS, Version 22.0, IBM Corporation, Armonk, NY). Continuous variables, such as Gensini score, retinal thickness, vessel density and flow area are presented as the means ± SD. The chi-square test and two-sample t-test were used to evaluate the differences between the two groups. Partial correlation analysis was used to assess the correlation between any two non-normally distributed variables. All p-values were two-tailed, and $p<0.05$ was considered statistically significant. Estimated odds ratios (ORs) and 95% confidence intervals (CIs) are presented for associations between Gensini scores and retinal or choroidal microvasculature (vessel density and flow area).

3. Results

3.1 Baseline

During the study process, 316 eligible participants (142 men and 174 women) contributed 632 ocular examinations (mean age: 65.1 ± 8.0; range: 36-87 years). Sex ratios were 72/86 (CHD

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group) and 70/88 (control group). In the CHD group, 109 (69.0%) patients had hypertension, and 35 (22.2%) had diabetes mellitus (DM). Age and sex showed no difference between CHD patients and controls (P = 0.64, 0.66). (Table 1)

Table 1. Clinical characteristics of the two groups

Clinical variables	CHD group Group A (n = 158)	Control group Group B (n = 158)	P-values
Age (years)	66.3 ± 8.4	64.4 ± 9.2	0.64
Male/Female	72/86	70/88	0.66
History of hypertension	109/158	N/A	-
History of DM	35/158	N/A	-

DM: diabetes mellitus

3.2 Changes in retinal thickness, vessel density, and flow area

The retinal thickness was thinnest in the foveal area (region), followed by the temporal area, for all subjects. The retinal thicknesses diameters in CHD patients in all eight regions were smaller than controls. However, all data did not show a significant difference between the two groups. A summary of the retinal thickness of eight regions in both groups is presented in Fig. 2 (The specific data is in Dataset 1, Table 2).

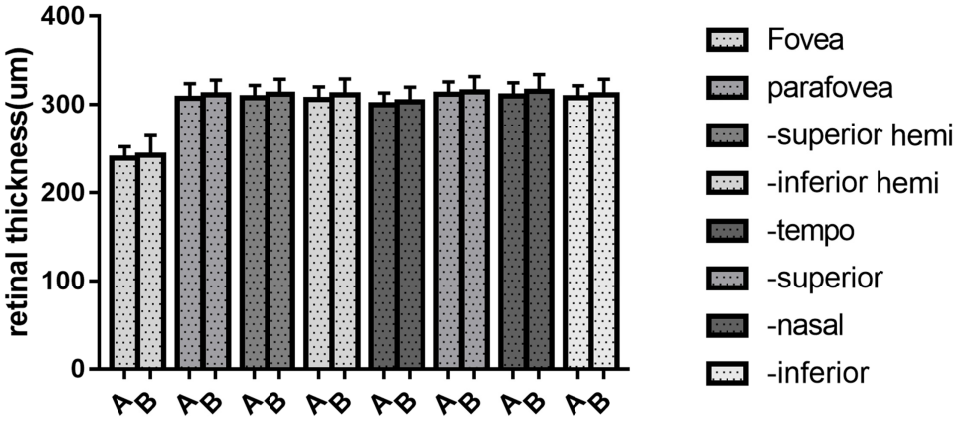

Fig. 2 The mean retinal thicknesses diameters (μm) in CHD patients (group A) and controls (group B) in eight regions.

Vessel density and flow area are the clearest reflection of fundus microvasculature by OCTA. When comparing group A and group B, the density and flow area of most zones showed a significant decreasing trend (P<0.05), except the superficial and deep fovea (P = 0.28, 0.20). Unexpectedly, CHD patients had more intensive vessel density in the outer retina (P<0.01) (Fig. 3, the specific data is in Dataset 1, Table 3).

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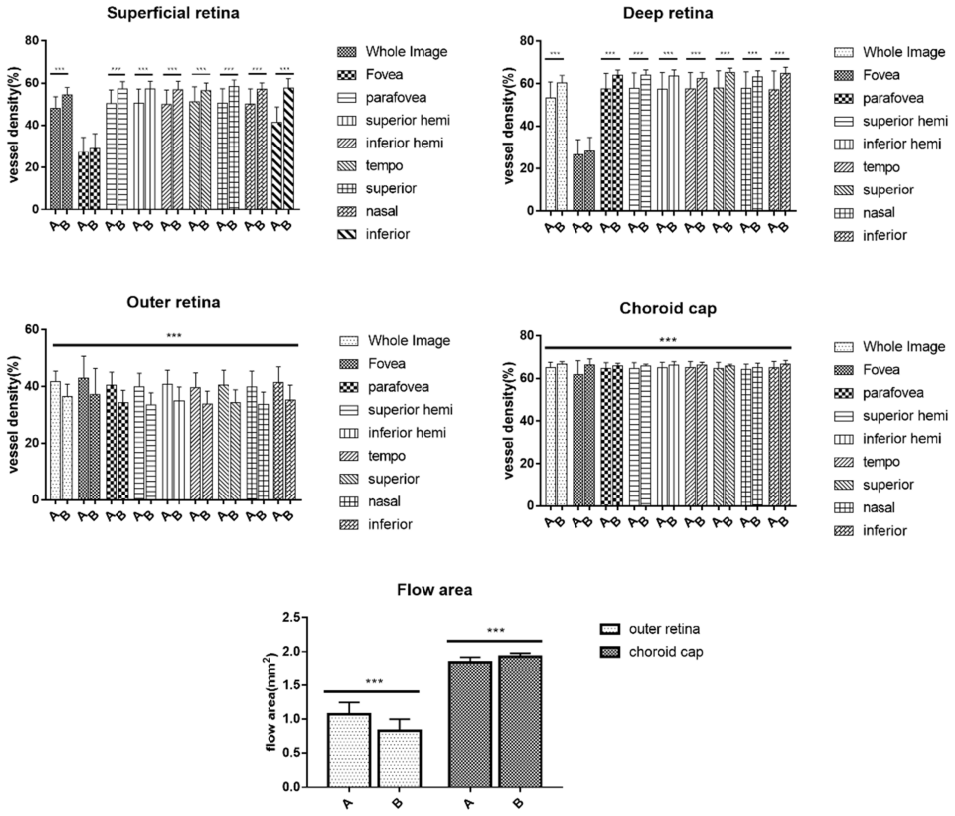

Fig. 3 The vessel density (four layers) and flow area (two layers) of CHD patients (group A) and controls (group B) (***: P<0.01).

3.3 Coronary artery stenosis affecting retinal and choroidal microvasculature

To further explore the potential effect of coronary artery stenosis on retinal and choroidal microvasculature, we investigated the correlation between every coronary artery branch Gensini score and fundus microvasculature change after correcting for age and sex.

3.3.1. Left main coronary artery (LMCA)

Pearson correlation analysis revealed that except for the fovea, all zones of superficial, deep vessel density, including the choroid capillary fovea and choroid capillary flow, exhibited a significant negative correlation with LMCA stenosis. As the main branch of the coronary artery, the LMCA stenosis affected most retinal vessels. An impressive result was the positive correlation between the outer retina (also except fovea zone) and LMCA score.

3.3.2. Left anterior descending branch (LAD)

We found that LAD proximal portion stenosis severity has a significant negative association with the deep retina (except fovea zone), choroid capillary fovea vessel density, and choroid capillary flow. As to mid-left and the distal portion, by contrast, the stenosis had no significant association with the vessel density and the flow area of all layers.

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3.3.3. Left circumflex coronary artery (LCX)

Patients with LCX proximal portion stenosis had the same microvasculature changes as those with LMCA stenosis. However, the distal portion had no significant difference in fundus vessels or flow, which was similar to the distal portion of LAD. For obtuse marginal (OM), one of the main branches of LCX, the stenosis severity had a negative correlation with deep vessel density (except the fovea zone) and choroid capillary flow.

3.3.4. Right coronary artery (RCA)

Although RCA weight (1.0) was much less than LMCA weight (5.0) in the Gensini score, the RCA proximal portion still had a significant impact on several zones of fundus vessel density (negative for the superficial and deep layer except fovea, positive for the outer retina layer except the fovea). In addition, the post-descending artery (PDA) had a significant negative correlation only with choroid flow (Table 2A-E, the specific data is in Dataset 1, Table 4 [38]).

Table 2. Association between retinal and choroid microvasculature and every branch Gensini score

2A

Super retina	LM	LAD (pro)	LCX (pro)	OM	RCA (pro)	PDA
W	-0.125*	-0.045	-0.169**	-0.108	-0.115*	-0.059
F	-0.027	-0.102	-0.043	-0.023	-0.080	-0.044
Para	-0.137*	-0.066	-0.208**	-0.111	-0.136*	-0.047
S-H	-0.129*	-0.063	-0.218**	-0.104	-0.117*	-0.054
I-H	-0.137*	-0.066	-0.189**	-0.102	-0.148*	-0.039
T	-0.150*	-0.099	-0.195**	-0.099	-0.169**	-0.033
S	-0.169*	-0.047	-0.199**	-0.103	-0.125*	-0.063
N	-0.149*	-0.044	-0.211**	-0.107	-0.179**	-0.041
I	-0.131*	-0.050	-0.162**	-0.107	-0.168**	-0.037

2B

Deep retina	LM	LAD (pro)	LCX (pro)	OM	RCA (pro)	PDA
W	-0.191**	-0.154**	-0.235**	-0.158**	-0.122*	-0.091
F	-0.090	-0.069	0.047	0.035	-0.016	0.003
Para	-0.189**	-0.159**	-0.268**	-0.16**	-0.127*	-0.056
S-H	-0.201**	-0.159**	-0.295**	-0.145*	-0.128*	-0.062
I-H	-0.167**	-0.150*	-0.227**	-0.160**	-0.137*	-0.048
T	-0.162**	-0.156**	-0.218**	-0.198*	-0.172*	-0.054
S	-0.173**	-0.136*	-0.291**	-0.160**	-0.124*	-0.062
N	-0.196**	-0.141*	-0.251**	-0.185**	-0.185**	-0.065
I	-0.154**	-0.143*	-0.208**	-0.131*	-0.169*	-0.024

2C

Outer retina	LM	LAD (pro)	LCX (pro)	OM	RCA (pro)	PDA
W	0.191*	0.050	0.156**	0.002	0.192**	0.004
F	0.004	-0.020	0.012	-0.071	-0.07	0.082
Para	0.126*	0.102	0.229**	0.059	0.127*	0.022
S-H	0.120*	0.085	0.224**	0.055	0.155*	0.031

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I-H	0.128*	0.108	0.214**	0.058	0.154*	0.013
T	0.123*	0.106	0.226**	0.028	0.192**	-0.005
S	0.128*	0.036	0.160**	0.074	0.186**	0.029
N	0.131*	0.087	0.234**	0.074	0.113	0.035
I	0.113	0.070	0.188**	0.035	0.150*	0.021

2D

Choroid capillary	LM	LAD (pro)	LCX (pro)	OM	RCA (pro)	PDA
W	-0.108	-0.061	-0.045	-0.109	-0.045	-0.093
F	-0.126*	-0.159*	-0.203**	-0.133*	-0.090	-0.051
Para	-0.089	-0.068	-0.076	-0.095	-0.054	-0.038
S-H	-0.081	-0.049	-0.069	-0.066	-0.068	-0.042
I-H	-0.910	-0.09	-0.082	-0.058	-0.028	-0.039
T	-0.107	-0.049	-0.084	-0.037	-0.032	-0.032
S	-0.021	-0.049	-0.075	-0.083	-0.064	-0.014
N	-0.083	-0.029	-0.026	-0.108	0.000	-0.077
I	-0.990	-0.108	-0.077	-0.105	-0.081	-0.018

2E

Flow area	LM	LAD (pro)	LCX (pro)	OM	RCA (pro)	PDA
Outer retina	0.059	0.051	0.061	0.041	0.033	0.058
Choroid capillary	1.127*	-0.181**	-0.167**	-0.162**	-0.056	-0.146*

4. Discussion

In this study, we examined retinal thickness, vessel density and flow area in normal and CHD individuals with OCTA and analyzed possible factors affecting retinal and choroidal microvasculature. Vessel density and flow area are the most intuitive reflection of fundus microvasculature by OCTA. When comparing group A and B, except for the superficial and deep fovea (P = 0.28, 0.20), the density and flow areas of most zones showed a significant decreasing trend (P<0.05). Unexpectedly, CHD patients had significantly more intensive vessel density in the outer retina. Our results show that fundus microvasculature changes might reflect the severity and progress of coronary artery lesion in CHD patients. Using OCTA, we found that some early-stage CHD patients can be defined as a high-risk population due to reduced retinal vessel density, choroidal vessel density and flow area. Therefore, OCTA is an efficient and noninvasive measurement method for detecting early-stage CHD. For these early-stage CHD patients, further examination or treatment methods, such as CAG and percutaneous transluminal coronary intervention (PCI), should be actively pursued to prevent myocardial infarction. Meanwhile, regular ophthalmic follow-up for these high-risk patients can also effectively decrease the morbidity of ocular complication.

Some studies have investigated the relationship between retinal vascular change and CAD or CHD. A study involving 109 CAD patients found that the degree of retinal arterial atherosclerosis was strongly correlated with the extent and severity of CAD [19]. A similar study on the correlation between retinal arteriolar narrowing and incident CAD in healthy middle-aged people supported this conclusion. This study also illustrated the more prominent microvascular role in the development of CHD. Other studies found that the diameter of retinal vessels, especially arterioles, may predict CAD or CHD risk and stroke-related deaths in middle-aged persons. It was concluded that microvascular change processes might have a role in CAD or CHD development [20–22]. All these studies were conducted after CHD patients showed clinical signs of fundus vascular changes. However, our study not only examined the shape of the retinal vasculature but also detected the retinal vascular density, choroidal vascular density, and blood flow area before the patients showed any clinical

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fundus sign. Subtle fundus vascular changes may reflect early cardiovascular diseases and help cardiologists make effective intervention measures. We expect that this would reduce the incidence of myocardial infarction at later stages.

Several probable mechanisms explain these conclusions. Atherosclerotic changes in the fundus vessels are related to the thickening of the microvascular wall and lipid precipitation, which are often associated with fibrosis and even with the calcification of larger arteries[19]. Thus, retinal arteriolar narrowing is considered an early indicator of microvascular damage. Because similar pathological features are also shown in the coronary artery of patients with CAD or CHD, changes in the retinal or choroidal microvascular may indicate changes in the systemic macrovasculature, especially in coronary artery stenosis.

Our results also showed that LMCA and LCX/RCA (proximal portion) stenosis had a positive association with the vessel density of the outer layers. The outer retina is avascular in healthy eyes. However, due to the high reflectivity of the RPE, images of the outer retina contain projection artifacts identical to the overlying vasculature from the superficial and deep plexus. Some retinal ischemic diseases, such as macular degeneration, retinal angiomatous proliferation (RAP), and macular telangiectasia, are associated with the hyper-reflective material in the outer retina. These features are highly susceptible to projection artifact and may lead to false-positive flow detection in the outer retina [18,23–28]. We also considered that hyper-reflective deviation created the positive correlation between outer retina vessel density and coronary artery branches.

The Gensini score, presented by Gensini GG in 1983, has been widely used for assessment of coronary artery stenosis. Gensini score gives a weighting factor for all branches according to their importance [20]. The LMCA has the highest weight, followed by LAD (proximal portion) and LCX (proximal portion). Follow-up research supported Gensini's view that the LMCA and LAD are the predominant vessels in cardiac blood supply [29]. In this study, we found that LMCA stenosis influenced most areas of retina and choroid, followed by the LAD and LCX. The RCA was also related to several fundus areas, which also supports Gensini`s viewpoint.

In this study, we found that higher Gensini score, which indicated greater coronary artery stenosis, was negatively associated with a particular area of retinal/choroidal vessel density and flow. More specifically, we found that LMCA stenosis and LCX/RCA (proximal portion) stenosis had significant negative associations with vessel density changes in the superficial, deep layers (except fovea zone) and choroid capillary fovea; the LAD (proximal portion) had a negative association with deep and choroid capillary fovea; CHD individuals with OM stenosis had thinner deep layers compared with normal controls. Furthermore, LMCA, LCX/LAD (proximal portion), OM, and PDA stenosis standard had negative associations with choroidal flow changes (Fig. 4).

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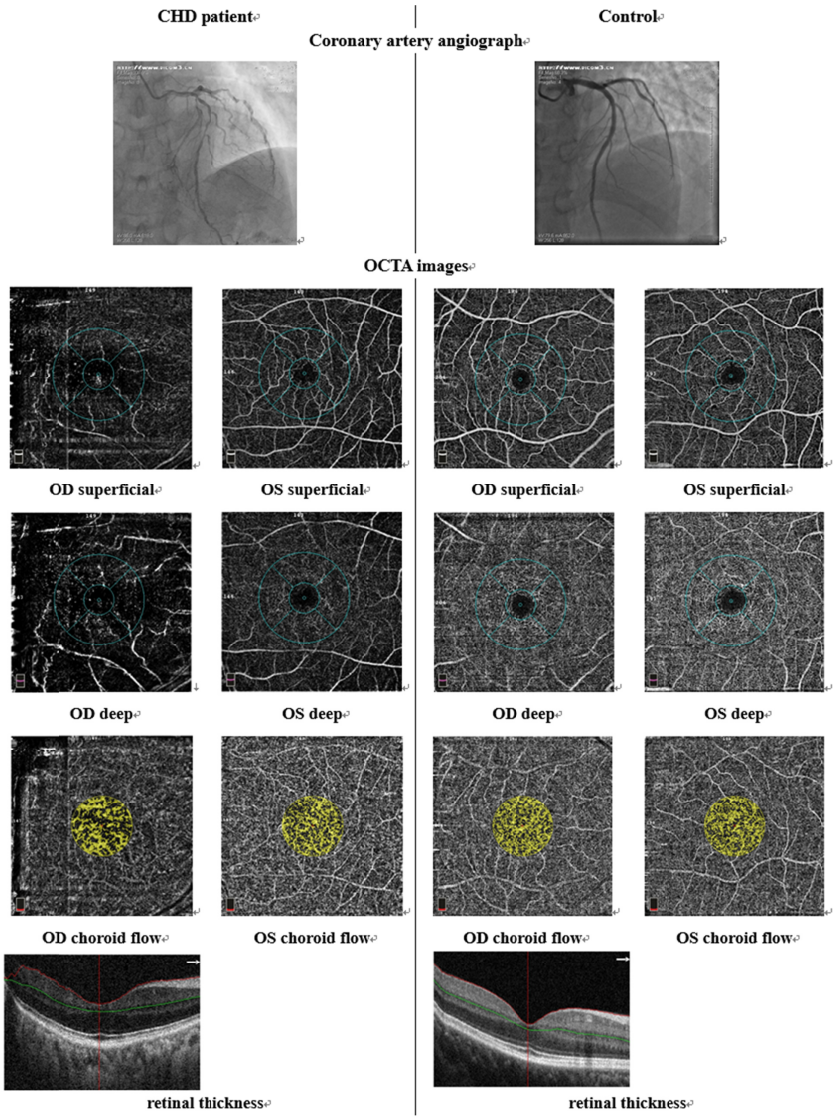

Fig. 4 Comparison of CAG and OCTA images between a CHD patient and control participant. Both vessel density (superficial and deep layers) and choroid flow decreased significantly when coronary artery stenosis occurred (participants' information has been hidden). The retinal thickness has no significant difference. (CHD patient: patient with coronary heart disease. Control: normal subject. Superficial: superficial layer of OCTA image. Deep: deep layer of OCTA image. OD: right eye. OS: left eye)

We suspect that for the fundus microvasculature, the LMCA, LAD, LCX (proximal portion, including OM) and RCA (including PDA) may have greater weights. To our knowledge, however, few studies have evaluated the correlation between retinal/choroidal blood supply and each branch of the coronary artery. Our study is the first to quantify all layers of fundus vessel density and flow area in a group of adults with CHD.

As a noninvasive tool, OCTA provides both structural (vessel density) and functional (blood flow) information in tandem. Moreover, compared with traditional FFA and indocyanine green angiography (ICGA), it appears to have a higher resolution than the currently available angiography images [30]. OCTA can detect the precise location of both retinal and choroidal microvasculature pathology, while FFA is used for seeing the retinal

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vessels, and ICGA is more suitable for imaging the choroid [31]. Fluorochromes may cause side effects, such as nausea, allergic reactions, and anaphylaxis.

Like FFA for retinal vasculopathy, coronary artery angiography (CAG) has been established as a gold standard for the investigation of cardiovascular diseases. However, because of injury, irritability, and side effects of the contrast agent, replacement of the invasive component for these investigations has become preferable in some circumstances [32]. Based on the above, coronary computed tomography angiography (CCTA) has become an additional tool for the assessment of coronary artery stenosis [33–36]. CCTA provides advantages over conventional angiography. However, CCTA is still completely unacceptable for a small number of sensitive patients. In this case, OCTA, a novel, noninvasive, drug-free examination method, may provide a solution for extremely sensitive or very early-stage patients without any clinical symptom, both in ophthalmology and in the cardiovascular system.

Although OCTA can provide valuable information and be applied to a broader population than other methods, it should be emphasized that ophthalmologists and cardiologists are still learning how and when to apply OCTA to assess vascular stenosis situations. For example, in contrast to FFA or ICGA, OCTA cannot identify abnormal vascular permeability, sclerosed/clotted microaneurysms, or hyporeflective intraretinal fluid pockets (typical performance of macular edema) because of the differences in the biologic phenomena [37]. Moreover, accurate outputs require highly refractive conditions, so severe cataract or vitreous hemorrhage may bias OCTA measurement. Thus, a conservative approach to the results of OCTA is warranted when making final treatment decisions.

The limitations of this study are the predominantly homogenous subject group (100% Asians from China), a relatively small sample size, and a lack of long-term follow-up, which may have increased the bias of the study. More extensive and longitudinal studies are necessary to verify these results.

In summary, we found that except for the superficial and deep fovea, vessel density in all retinal/choroidal layers and choroidal flow area decreased in CHD patients without any ophthalmologic clinical signs. LMCA, LCX/RCA (proximal portion), LAD (proximal portion), OM, and PDA stenosis were associated with the diminishing of different retinal layers in this study. Our results suggest that the vascular damage of the retina may occur early, before visual impairment, in CHD individuals. Moreover, OCTA is a valuable and accurate diagnostic tool for providing detailed vascular measurements of the retina or choroid to detect early lesions of the retina and choroid in CHD patients.

5. Conclusion

With OCTA, we detected that except for the superficial and deep fovea, vessel density in all retinal/choroidal layers and choroidal flow area decreased before any clinical fundus sign showed in CHD patients. We found that retinal and choroidal microvasculature changes were closely related to coronary artery and branch stenosis. For instance, LMCA, LCX/RCA (proximal portion), LAD (proximal portion), OM, and PDA stenosis were all associated with diminishing vessel density and flow area. Furthermore, we demonstrated that OCTA is an efficient and noninvasive measurement method for detecting early-stage CHD, which can reduce the incidence of myocardial infarction at later stages. Further randomized trials with larger patient groups and additional systemic parameters could shed more light on this issue.

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Disclosures

None of the authors have any financial/conflicting interests to disclose.

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